



PCT/GB99/01550

## REPLACED BY ART 34 AMDT

## **CLAIMS**

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A compound of formula:

Y-(CR<sub>2</sub>)<sub>n</sub>-X-NHJ

5 where:

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residue.

X is C=O or CR<sub>2</sub>;

n is an integer of value 1 to 6;

Y is L(A)<sub>m</sub>- or R¹R²CR-where L is a metal complexing agent,

A is -CR $_2$ - , -CR=CR- , -C≡C- , -NRCO- , -CONR- , -SO $_2$ NR- ,

-NRSO<sub>2</sub>- , -CR<sub>2</sub>OCR<sub>2</sub>- , -CR<sub>2</sub>SCR<sub>2</sub>- , -CR<sub>2</sub>NRCR<sub>2</sub>- , a C<sub>4-8</sub> cycloheteroalkylene group, a C<sub>4-8</sub> cycloalkylene group, a C<sub>5-12</sub> arylene group, a C<sub>3-12</sub> heteroarylene group or a polyalkyleneglycol, polylactic acid or polyglycolic acid moiety;

m is an integer of value 0 to 10;

where one of R¹ and R² is -NH(B) $_pZ^1$  and the other is -CO(B) $_aZ^2$  where

p and q are integers of value 0 to 45, and each B is independently chosen from Q or an amino acid

where Q is a cyclic peptide;

Z¹ and Z² are protecting groups;

J and each R group are independently chosen from H,  $C_{14}$  alkyl,  $C_{14}$  alkenyl,  $C_{14}$  alkynyl,  $C_{14}$  alkoxyalkyl or  $C_{14}$  hydroxyalkyl; with the provisos that:

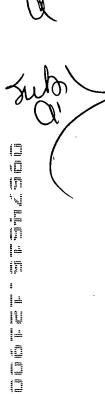
- 25 (i) the total number of amino acid residues in the R¹ and R² groups does not exceed 45;
  - (ii) when X is CR<sub>2</sub>, then Y is -CRR<sup>1</sup>R<sup>2</sup> and Z<sup>2</sup> is a metal complexing agent;
- (iii) when Y is -CRR¹R² then at least one of R¹ and R² bears at least one detectable moiety.



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- The compound of claim 1 where R1 or R2 includes one or 2. more peptide fragments of  $\alpha_2$ -antiplasmin, fibronectin, beta-casein, tetanus, amyloid, trappin and polyglutamine residues, said peptide fragment containing at least three amino acid residues.
- 3. The compound of claim 2 where the peptide fragment is from  $\alpha_2$ -antiplasmin.
- The compound of claim 3 where the amino acid in the 2-4. position from the peptide N-terminus is glutamine. 10
  - 5. The compound of claim
- 6. The compound of claim 5 of formula: Y-(CR<sub>2</sub>)<sub>x</sub>-(CH<sub>2</sub>)<sub>2</sub>CONH<sub>2</sub> or Y-(CR<sub>2</sub>)<sub>y</sub>-(CH<sub>2</sub>)<sub>4</sub>NH<sub>2</sub> 15 where x is an integer of value 0 to 4, and y is an integer of value 0 to 3.
  - 7. The compound of a -CRR<sup>1</sup>R<sup>2</sup>.
  - 8. The compound of any on of Z<sup>1</sup> and Z<sup>2</sup> is a metal complexing agent.
- The compound of claim 8 where Z<sup>2</sup> is a metal complexing 9. agent and Z1 is not a metal complexing agent. 25
  - A metal complex of the compounds of claim 8 or claim 9. · 10.
- 11. The metal complex of claim 10 where the metal is a radiometal. 30



12. The radiometal complex of claim 11 where the radiometal is 99mTc.

13. A preparation for human administration comprising the compound of any one strains 1 to 12.

14. A kit comprising the compound of any one of claims 1 to 9 useful in the preparation of the metal complexes of any one of claims 10 to 12.

15. Use for the diagnosis of sites of thrombosis or embolism of a compound of formula:

Y-(CR<sub>2</sub>)<sub>n</sub>-X-NHJ

where:

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X is C=O or CR<sub>2</sub>;

n is an integer of value 1 to 6;

Y is L(A)<sub>m</sub>- or R<sup>1</sup>R<sup>2</sup>CR-where L is a metal complexing agent,

A is  $-CR_2$ -, -CR=CR-,  $-C\equiv C$ -, -NRCO-, -CONR-,  $-SO_2NR$ -,

-NRSO $_2$ - , -CR $_2$ OCR $_2$ - , -CR $_2$ SCR $_2$ - , -CR $_2$ NRCR $_2$ - , a C $_{4-8}$ 

cycloheteroalkylene group, a C<sub>4-8</sub> cycloalkylene group, a C<sub>5-12</sub> arylene group, a C<sub>3-12</sub> heteroarylene group or a polyalkyleneglycol, polylactic acid or polyglycolic acid moiety;

m is an integer of value 0 to 10;

where one of R1 and R2 is -NH(B),Z1 and the other is

25 –CO(B)<sub>q</sub>Z<sup>2</sup> where

residue,

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p and q are integers of value 0 to 45, and each B is independently chosen from Q or an amino acid

where Q is a cyclic peptide;

Z¹ and Z² are protecting groups;

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J and each R group are independently chosen from H,  $C_{14}$  alkyl,  $C_{14}$  alkenyl,  $C_{14}$  alkynyl,  $C_{14}$  alkoxyalkyl or  $C_{14}$  hydroxyalkyl; with the provisos that:

- (i) the total number of amino acid residues in the R¹ and R² groups does not exceed 45;
  - (ii) when X is CR<sub>2</sub>, then Y is -CRR<sup>1</sup>R<sup>2</sup>;
  - (iii) when Y is -CRR¹R² then at least one of R¹ and R² bears at least one detectable moiety.
- 16. Use for the diagnosis of sites of thrombosis or embolism of a radiometal complex of the compound defined in claim 13, wherein at least one of Z¹ and Z² is a metal complexing agent.
- 17. A peptide fragment of α₂-antiplasmin, fibronectin, beta 15 casein, tetanus, amyloid, trappin or polyglutamine, said peptide fragment containing 3 45 amino acid residues and carrying a terminal metal complexing agent.
- 18. The peptide fragment of claim 17, wherein the metal complexing agent is at the carboxy terminus.
  - 19. A metal complex of the peptide fragment of claim 17 on claim 18.

